



Antimicrobials in the Environment = *Less-Recognized Issues and Needs* <

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"Emerging" Pollutants?

The occurrence of pharmaceuticals and personal care products (PPCPs) in the environment is undoubtedly NOT a newly emerging phenomenon. Rather, it is one that has been made more widely evident (during the last decade) because continually improving chemical analysis methodologies have lowered the limits of detection for a wide array of trace xenobiotics in environmental matrices. Antibiotics constitute only but one of many broad classes of PPCPs, each of which poses its own unique concerns.

No reason to believe that certain PPCPs have not had a steady presence in the environment since they were first introduced to commerce.

PPCPs have been recognized as potential environmental pollutants by various scientists and government agencies (such as the U.S. FDA and EPA) since the 1970s. But the topic did not gain wider recognition by environmental scientists or by the public until the late 1990s. So in this sense, the issue is "emerging" only in terms of widespread discussion or recognition - - NOT in the sense of a new environmental phenomenon.

EPA's Role with PPCPs

EPA's involvement with the larger issue of **pharmaceuticals and personal care products (PPCPs)** as environmental pollutants is driven by a number of scientific concerns as well as three major regulatory mandates. Via the mandates, desired environmental and public health outcomes regarding PPCPs as pollutants can be achieved by the following process:

Regulatory Mandates:

- *Safe Drinking Water Act* (SDWA, 1974 & 1996) [in part, requires EPA to establish a list of contaminants (CCL) to aid in priority-setting for the Agency's drinking water program]
- *Clean Water Act* (CWA, 1972) [relevant to PPCP occurrence in, and removal from, sewage treatment works - STWs]
- *Resource Conservation and Recovery Act* (RCRA, 1976) [relevant to disposal of certain PPCPs; e.g., reverse distributors]
- *Federal Insecticide, Fungicide, and Rodenticide Act* (FIFRA, 1948) [e.g., orchard antibiotics, broad-spectrum biocides, emergency exemptions]

EPA's Role with PPCPs

Science Drivers Include Identification of:

- “Hidden”, previously unrecognized, or “emerging” environmental concerns before they become critical
- Potential (future) environmental concerns (anticipatory research)
- Pivotal sources of uncertainty that affect assessment of risk to human health and ecological integrity

Timely & Sound Science Allows for:

- **Proactive** vs. Reactive involvement — **Pollution prevention** vs. remediation/restoration
- Informed rules, decisions, or guidance

Necessary R&D Accomplished by:

- EPA in-house research (ORD and Program Offices, primarily Office of Water, Office of Solid Waste, Regions)
- EPA external research (e.g., STAR grants)
- Fostering interdisciplinary research and collaboration among academe, private sector, government - - nationally and internationally

EPA's Role with PPCPs

Supporting Data Collected via:

- EPA monitoring programs (e.g., under Contaminant Candidate List - CCL)
- Other agencies (e.g., USGS), academe, and industry

Necessary Environmental & Public Health Outcomes Achieved by:

- Changing consumer behavior (outreach programs and education)
- Effective communication of risk (cognitive sciences play key role)
- Voluntary stewardship programs (currently non-existent for PPCPs)
- Formal rules, decisions, guidance

Context & Perspective

The most visible concerns regarding the use and mis-use of antibiotics and their subsequent release as environmental pollutants involve: (i) selection for resistance among both apathogenic (e.g., commensal) and pathogenic bacteria and (ii) the horizontal transfer of intrinsic and extrinsic resistance genes to and among pathogens.

While these two topics are frequently debated, **a number of less-discussed or under-appreciated issues and questions underlay these concerns**. Many of these same issues are also pertinent to a wide spectrum of other PPCP classes (and transformation products) that gain entry to the environment by the same routes - - via direct discharge/disposal and by excretion.

These **less-discussed issues and questions**, as well as some attendant **research needs** are summarized in the following slides.

Summary of Less-Recognized **ISSUES**

EXPOSURE-Related Issues

- Many additional origins (*see slides 20-21*) exist for antibiotics in the environment other than CAFOs and sewage systems (but their relative significance is unknown)
- Introduction of antibiotics to the environment via continual sewage discharges imparts a "**pseudo-persistent**" quality to all constituent pollutants regardless of structural instability (environmental half lives become less important)
- Could monitoring data based on dissolved concentrations in water yield environmental-load estimates **biased low**? (because of "**hidden reservoirs**," such as conjugates and residues concentrated by partitioning to solids)

Summary of Less-Recognized *ISSUES*

- Could **microenvironments** and **niches such as interfaces** (e.g., biofilms) serve to maximize exposure concentrations as well as resistance-gene selection and horizontal transfer?
- Distribution of antibiotics to sewage sludge (and ultimately "biosolids") and manure is poorly understood and **cannot be predicted by lipophilicity alone** (because of other partitioning mechanisms)
- **Molecular farming** ("biopharming") may pose risks with regard to both resistance-gene transfer as well as serving as an uncontrollable source for environmental exposure to antibiotics themselves

Summary of Less-Recognized **ISSUES**

- Relative and absolute contribution from each of the various sources to the total environmental loads of individual and overall medicinal antibiotics are unknown; the underlying significance of **naturally occurring antibiotics** is especially unknown.
- Comprehensive picture is not available of the types, concentrations, distributions, and prevalence of antibiotics in the environment.
- **Target-based environmental monitoring** necessarily yields a filtered view of environmental occurrence by neglecting an unknown portion of unidentified constituents (*see slides 24-30*).

Summary of Less-Recognized **ISSUES**

EFFECTS-Related Issues

- Concern with regard to **alteration of microbial community structure** (with ramifications for trophic-level dynamics, e.g., via predator-prey interactions and species communication). **Two perspectives: Selection for resistant pathogens and discrimination against sensitive commensal microbes** (creating vacant niches).
- One of the proposed mechanisms of growth-promotion by sub-therapeutic administration is alteration of the gut's autochthonous microbiota. Such a mechanism points to the possibility of also altering microbial community structures in ecological niches via **hormetic response** as opposed to growth suppression
- Wide array of **non-antibiotics** (some of which have no inherent toxicity of their own) hypothetically could contribute to the development of both antibiotic resistance as well as susceptibility to low concentrations (*see slide 23*)

Summary of Less-Recognized *ISSUES*

- Many unknowns associated with exposure to mixtures of low levels of individual antibiotics (**interactive effects** such as additivity and synergism across wide spectrum of mechanisms of action, **hormetic responses** [both inhibitory and stimulatory]). Concern for aquatic environment with **continual, multi-generational exposure to complex mixtures of low-level toxicants**.
- Low levels of antibiotics in environmental waters may be irrelevant with regard to resistance selection, as key niches exist (serving as microbial reactors or "**cauldrons**") where microbial diversity and biomass coupled with higher (undiluted) antibiotic concentrations exist (e.g., communal septic systems and sewage trunk lines serving many people)

Summary of Less-Recognized *ISSUES*

- Non-target-species receptor repertoires are not well characterized. **Variation in receptor repertoires across species** confounded by unknown overlap with those of humans leads to countless questions regarding potential for **unforeseen effects**. MOAs not fully understood even for humans. **Most drugs can each have a multitude of effects**, many yet remaining to be discovered.
- What is environmental prevalence of loss of antibiotic resistance from bacterial populations after removal of selective pressure of antibiotic exposure? **Over-expression of broad-spectrum efflux pumps, "plasmid-addiction" systems, and exposure to naturally produced antibiotics may conserve resistance in the absence of continued "anthropogenic" selective pressure.**
- Broad-spectrum biocides/disinfectants (e.g., triclosan) could lead to selection for resistance to narrow-spectrum antibiotics.

Summary of Less-Recognized *NEEDS*

- **Historical disconnect between Human Health and Ecological Health** persists. Must transition away from reductionist approach to a holistic understanding. Many benefits could accrue to the consumer and the environment alike (key aspect of "cradle-to-cradle" stewardship programs)
- Examination of the usefulness of assessing the risk of individual toxicants in isolation from all others (“**exposure totality**”) and without regard to exposure history (“**trajectory**”)
- **National Research Strategy** and priorities regarding PPCPs as pollutants. Currently, many federal agencies are playing roles in PPCP research (CDC, USDA, USEPA, USFDA, USFWS, USGS). Is there need to integrate with efforts underway with non-US entities (Health Canada, EMEA, various EU committees, Danish EPA, etc.)?

Summary of Less-Recognized *NEEDS*

- Potential regulations requiring environmental chemical monitoring should consider basing monitoring programs on **evolutionarily conserved biochemical features and MOAs** rather than on individual chemical entities. Such an MOA-based approach could include assays measuring inhibition/induction of cellular stress response (e.g., HSP with coupled ubiquitin-proteasome pathway), CYP (cytochrome P-450), multi-drug transporters (efflux pumps). This could be the best way to automatically account for (i) a multitude of stressors sharing a common MOA (cumulative exposure) and (ii) stressors newly introduced to commerce.
- **Non-culturable microbes** impede determining prevalence of antibiotic resistance. Do they also serve as a significant but unidentifiable reservoir of resistance genes?
- More realistic susceptibility testing methods. For example, **intrinsic in vivo antibiotic resistance can be masked by in vitro antibiotic sensitivity** (e.g., protection of sensitive variants conferred by small numbers of resistant variants, such as by pH alteration of microenvironment).

Summary of Less-Recognized *NEEDS*

- Important to foster communication between scientists and regulators across the **historically separated medical and environmental arenas**
- **Nationwide early-warning chemical monitoring system for waters** (detection of emerging pollutants)
- **Real-time GIS database for nationwide PPCP usage** (important for gauging absolute usage and geographic variabilities)

Summary of Less-Recognized **NEEDS**

- Imperative to integrate cognitive sciences (e.g., psychology) in the communication of risk (and improving science literacy for the laity). Effective communication of science is also critically important not just to ensure the continued support of science but also to ensure that science plays its due role in the development of policy and the broader social agenda.
- Environmental stewardship (e.g., pollution prevention) programs are conspicuously absent for PPCPs. Near-term pollution prevention efforts are feasible for lessening the overall introduction of PPCPs to the environment (*e.g., see slide 43*)
- Aim for consensus on what role (if any) the Precautionary Principle should play in guiding environmental stewardship programs for drugs

Discussion of Less-Recognized Issues, Questions, and Needs Concerning Antibiotics in the Environment

The remaining slides expand upon
the points summarized in the
preceding slides

Human Health versus Ecological Health

Reductionist view must give way to holistic understanding

Social, scientific, engineering, and regulatory systems traditionally divide and separate what is really one integral system. The health of humans and the ecology are intimately intertwined.

A profound disconnect has long prevented progress in treating human and ecological health as one and the same.

Human Health versus Ecological Health

Scientists and regulators in the human and domestic animal health communities have traditionally been disconnected from those in the environmental arena.

Two major ramifications:

- (1) Knowledge is not shared across disciplines; intersecting literatures are rarely explored
- (2) Accountability is often absent for issues emanating from the interface of human medicine and the environment (important issues, especially those of regulatory nature, can “fall through the cracks”)

Origins and Significance of Antibiotics in the Environment

Well recognized that antibiotics in the environment originate from sewage treatment plants (ppb from human usage and direct disposal of expired product) and from CAFO waste (sub-ppm in lagoons).

But other sources also exist: sewage sludge ("biosolids") applied to land, medicated pet excreta, direct dispersal and loss from aquaculture, spray-drift from agriculture, direct discharge of raw sewage (storm overflow events and residential "straight piping"), sewage discharge from cruise ships (millions of passengers per year), and transgenic production of proteinaceous therapeutics by genetically altered plants (aka "molecular farming" - - "biopharming").

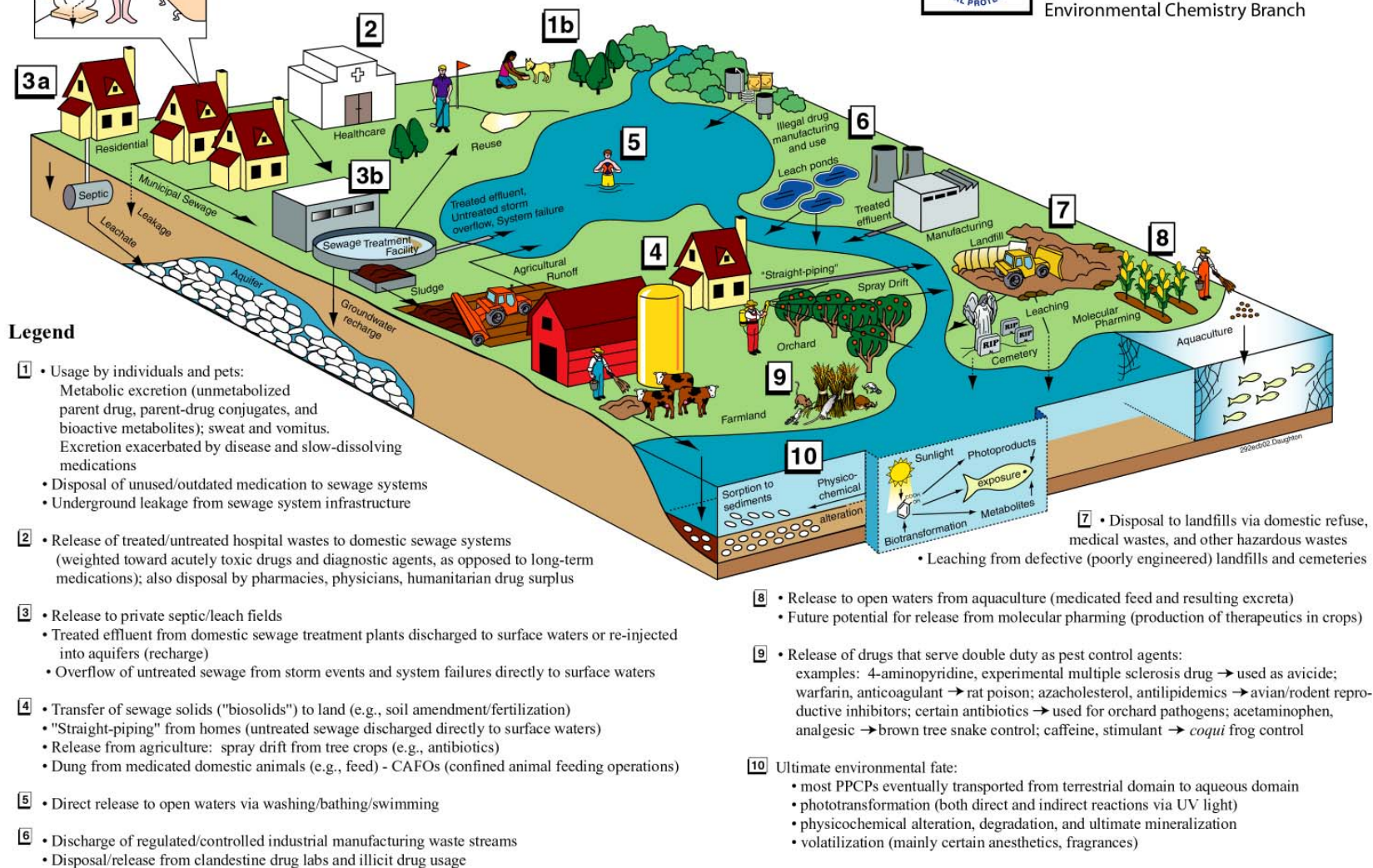


Origins and Fate of PPCPs[†] in the Environment

[†]Pharmaceuticals and Personal Care Products



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Origins and Significance of Antibiotics in the Environment

Significance of antibiotic occurrence in the environment is not known.

Can resistance in bacteria be selected for by sub-therapeutic concentrations?

Can resistant human pathogens be selected for or created by genetic transfer outside host organisms in the environment?

Can microbial community structure (or trophic-level dynamics, predator-prey interactions and balance, species communication) be altered? Possible importance of low concentrations, especially for key prokaryotes such as cyanobacteria (e.g., *Microcystis*), where lethality EC50s can approach 1 ppb for various antibiotics. Because many antibiotics tend to be protic, the pH during exposure is critical (low pH favoring membrane permeability for anionic antibiotics).

Do not know the relative roles that might be played by each source in contributing to the total environmental loads of individual medicinal antibiotics, of combined medicinal antibiotics, or of overall **medicinal** and **naturally occurring antibiotics**.

Unknowns: Promotion of Antibiotic Resistance by Non-Antibiotics

Hypothetically, antibiotic resistance can be temporarily promoted by exposure to non-antibiotics (even chemicals having no inherent toxicity) that induce over-expression of general cellular protective strategies:

One example: induction of p-glycoprotein multi-drug resistance efflux systems (MDR/MDX)

Likewise, the inhibition of MDR could hypothetically lead to increased susceptibility to antibiotics at low concentrations.

Unknowns: Prevalence of Antibiotics in the Environment

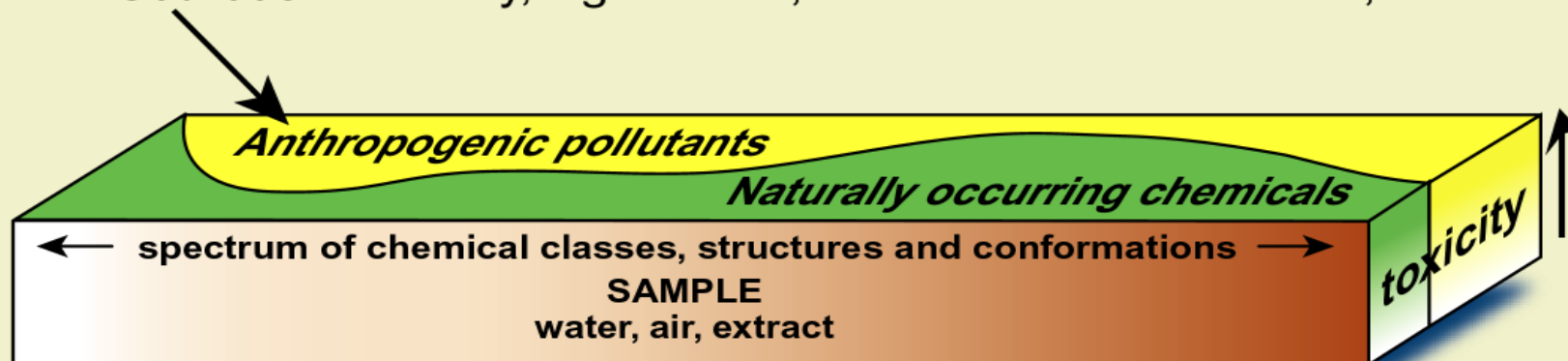
Comprehensive picture of the types, concentrations, distributions, and geographic prevalence of antibiotics in the environment is not available.

Attaining a more comprehensive picture is prevented by the nature of “**target-based**” chemical monitoring (in contrast to laborious but comprehensive **chemical characterization**).

This same limitation applies to PPCPs in general.

Universe of Chemicals in the Environment

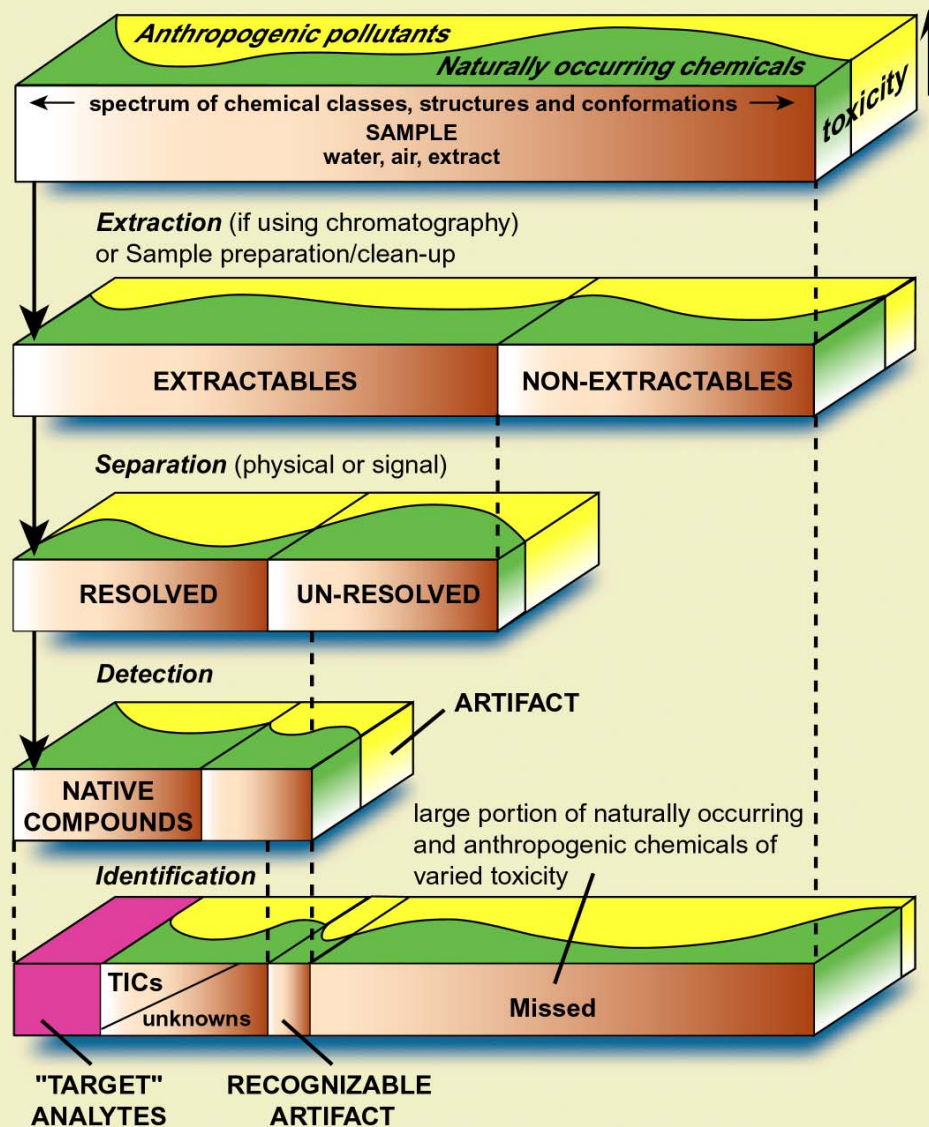
Sources: Industry, Agriculture, Household Maintenance, PPCPs



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Limitations and Complexity of Environmental Chemical Analysis

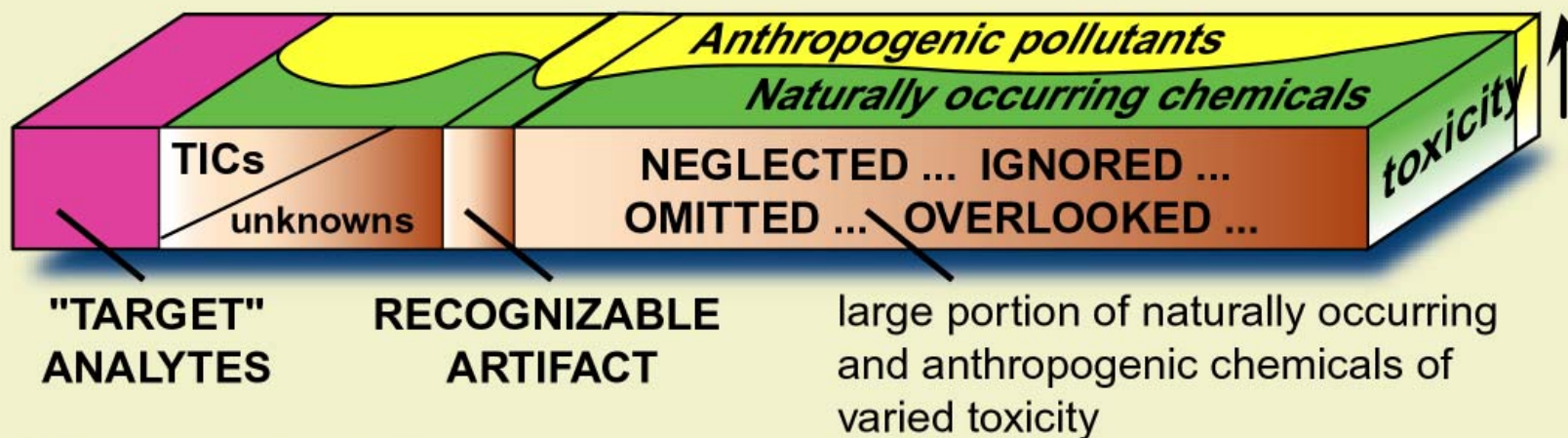


TICs = tentatively identified compounds

C.G. Daughton
U.S. EPA July 2002
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Chemical Analysis Output for a Typical Environmental Sample



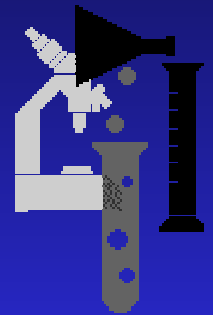
TICs = tentatively identified compounds

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Einstein on: *Environmental Monitoring*

“Not everything that can be counted counts,
and not everything that counts can be
counted.” (oft attributed to Albert Einstein)



corollary for environmental monitoring

**Not everything that can be measured is
worth measuring, and not everything
worth measuring is measurable.**

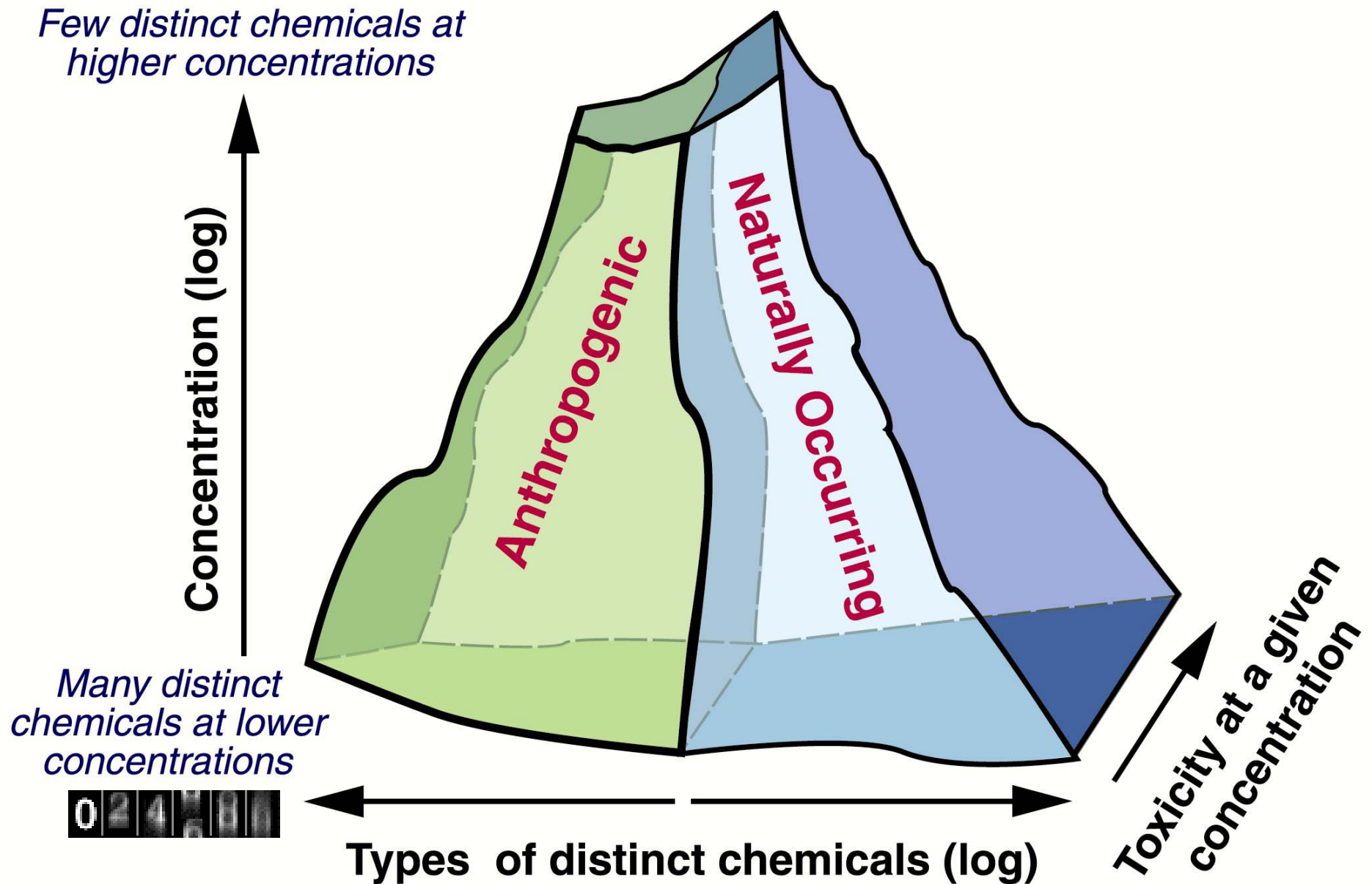


Prevalence of Xenobiotic Occurrence: Some Possible Generalizations Regarding Ubiquity

- The lower the concentration, the higher the probability of larger numbers of distinct chemicals occurring
- **Exponentially more types of chemicals occur at exponentially lower concentrations** (*does the distribution of chemical types versus their concentrations follow a power law, as shown for such a wide array of other phenomenon? e.g., see: M. Buchanan "Ubiquity", Crown Publishers 2000*)
- At the very lowest concentrations (zeptomolar to yoctomolar, zM - yM), the off-the-cuff truism may apply:

"Everything can be found everywhere"

Prevalence/Distribution of Xenobiotic Occurrence



Unknowns: Relative Importance of Suspended versus Non-Suspended Bacteria

Most gene-transfer studies focus on suspended bacteria (e.g., in wastewaters).

Little attention devoted to possibly more important niches where the probability of gene transfer could be maximized - - where both bacteria and antibiotics might be more concentrated.

Biofilms (esp. in drinking water distribution lines and bank filtration areas) may improve horizontal transfer of resistance genes (both intrinsic and acquired) between autochthonous-allochthonous consortia .

Unknowns: Relative Importance of Suspended versus Non-Suspended Bacteria

Biofilms have two inherent features favorable to horizontal transfer lacking in suspended niches:

- (1) higher diversity of microbial genera and species
- (2) much greater biomass

Can ubiquitous apathogenic microbes with intrinsic or acquired resistance pass genes to pathogens?

[ref: "Detection of antibiotic-resistant bacteria and their resistance genes in wastewater, surface water, and drinking water biofilms," *FEMS Microbiology Ecology*, in press, available online 23 November 2002. Thomas Schwartz, Wolfgang Kohnen, Bernd Jansen and Ursula Obst]

Unknowns: Relative Importance of Dissolved versus Non-Dissolved Concentrations

While concentrations of antibiotics at STWs and in the environment might be orders of magnitude below "therapeutic" levels (with the implicit assumption that these concentrations are too low to select for bacterial resistance), **it is critical to remember that at the origin of a waste conveyance line, the concentrations of antibiotics will be orders of magnitude higher because of less dilution.**

Such critical niches might provide sufficient "reactor" time to maximize contact among a diversity of microorganisms and antibiotics from a wide spectrum of people.

Unknowns: Do Cauldrons of Resistance-Selection and Horizontal Transfer Exist?

Assuming that horizontal transfer is maximized where high diversity and biomass of microbes co-exist with a multitude of antibiotics possessing similar and different mechanisms of action:

Horizontal transfer might be expected to be maximized in:

- communal septic systems used by numerous people.
- sewage trunk lines close to manifolds from numerous origins
- sewage sludge

These niches could be serving as “cauldrons” for ensuring optimal microbial contact with the highest concentration and diversity of antibiotics (and other PPCPs acting in synergy) as well as for optimizing the horizontal exchange of genetic material.

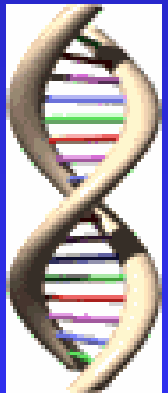
Unknowns: Special Cauldron Created by Molecular Farming ("Biopharming")

Many risks posed by bioengineered pharmaceutical plants. [transgenic biotechnology currently has the potential for using genetically altered food crop species (primarily corn, soybeans, rice) for producing hundreds of distinct proteinaceous therapeutics (including enzymes, hormones, monoclonal antibodies, in addition to drugs).]

Molecular farming of antibiotics is but one concern, and it has several dimensions.

Crops engineered to produce pharmaceuticals have the potential to lead to:

- inadvertent exposure of humans to the pharmaceutical itself (via cross contamination within food crops),
- exposure of wildlife by foraging and processing detritus,
- horizontal transfer of antibiotic-resistance marker genes (used for monitoring success in transgene transfer to the crop) to bacteria in the environment, and
- horizontal resistance-gene transfer within the mouth or elsewhere in the gut by ingestion of antibiotic-resistance marker genes



Unknowns: Bias of Monitoring Data

Caveats: Analysis of Waters for Drugs

High water solubility of most drugs can lead to a biased focus on the water column. Measurement of dissolved water concentrations of parent chemical can mislead by yielding underestimates of environmental loads.

Hidden “Reservoirs” (compartments not accounted for by water analysis):

- hydrolysis of excreted conjugates can be reconverted back to parent forms
- desorption from sediments/suspended particulates
- dissolution of poorly soluble forms (e.g., divalent cations-polyprotic tetracyclines)

Unsuspected Environmental Compartments

- conveyance to land via biosolids or to sediments via particulates

Bias of Analytical Methodologies (especially sample prep & extraction):

- low, uncorrectable analytical recoveries

Does calculating total environmental loads via aqueous-dissolved quantities possibly yield estimates of total loads or burden orders of magnitude too low?

Each of these points could apply to various classes of antibiotics.

Unknowns: Complete Picture of Microbial Exposure to Antibiotics

Chemical Measurements and Exposure Reality

Dissolved concentrations (or even total solids loadings) may not represent actual exposure concentrations, especially for microorganisms.

- In microbial settings, much happens in the microenvironment of **interfaces**.
- Interface chemistry does not necessarily reflect dissolved chemistry.
- Concentrations of stressors can be substantially higher at an interface (for example the surface of a biofilm).
- Consequences of heterogeneous distribution could be profound. For example, bacteria could be exposed to higher concentrations of antibiotics than projected from water concentrations, perhaps high enough to select for resistance or change community species structure.

Needs: Research Coordination

Is there need for an inter-agency forum to discuss the many issues associated with PPCPs as pollutants?

To identify knowledge gaps and set research priorities?

Is there a need to develop an overarching *National Research Strategy* to coordinate research across government, industry, and academe?

Or is the current rate of advancement sufficient?

Important to foster communication across the disparate fields of medical, health-care, and environmental sciences.

Importance of Forging Collaborations between Environmental Scientists & Medical Community

- Existing literature almost exclusively a result of efforts from environmental scientists (primarily analytical chemists).
- Much could be contributed from the many fields of medical science and practice.
- Cross-communication and collaborations would prove extremely useful.
- Partly in an attempt to catalyze inter-disciplinary efforts, the British medical journal *The Lancet* recently published a commentary that covers this topic and others:

“Environmental stewardship and drugs as pollutants”
(C.G. Daughton), *The Lancet*, 2002, 360:1035-1036

Needs: Real-Time Database for Nationwide PPCP Usage

- Real-time, accurate data on nationwide drug-usage (and disposal) are unavailable to researchers and regulators.
- Neither the absolute usage rates for PPCPs nor their geographic variations are known. [Geographic drug usage patterns are partly a function of local prescribing customs and patient preferences.]
- For antibiotics, the absolute and relative usage among humans and domestic animals is not even accurately known.

Needs: Real-Time Database for Nationwide PPCP Usage

- First-ever study published on geographic variation of prescription drug usage: *Prescription Drug Atlas* (Express Scripts, 2001) [available at: http://www.express-scripts.com/other/news_views/outcomes_research/atlas2002/atlas_ex_sum.htm]
- Wide variations in geographic usage points to a potential problem with the way in which EECs/PECs are calculated.
- Real-time GIS database showing drug usage by geographic locale would greatly aid modeling and monitoring efforts; but the proprietary nature of the pharmaceutical industry and widespread OTC availability of agricultural antibiotics are major barriers.

Needs: Nationwide Early Warning Chemical Monitoring System

Integrated **nationwide early-warning water monitoring system** would simultaneously serve four key purposes:

- (1) Timely elucidation of newly emerging (previously unrecognized) pollutants,
- (2) Uncover trends in pollutant geographic distribution, prevalence, and loads
- (3) Provide objective geographic data on emerging trends in drug abuse and illicit drug use, and
- (4) Provide early warning of chemical sabotage agents in source waters.

Needs: Environmental Stewardship

Pollution prevention and other aspects of environmental stewardship are conspicuously absent for PPCPs.

The many, complex aspects of this topic are covered in a holistic manner for the first time - - in a two-part paper:

- Daughton CG. "Cradle-to-Cradle Stewardship of Drugs for Minimizing Their Environmental Disposition while Promoting Human Health - - Part I: Rationale and Avenues toward a Green Pharmacy," *Environmental Health Perspectives* (accepted Oct. 2002)
- Daughton CG. "Cradle-to-Cradle Stewardship of Drugs for Minimizing Their Environmental Disposition while Promoting Human Health - - Part II: Drug Disposal, Waste Reduction, and Future Direction," *Environmental Health Perspectives* (accepted Oct. 2002)

An initiative has been proposed with the EPA's Office of Solid Waste to further explore the use of pharmaceutical reverse distributors for minimizing the disposal of PPCPs to the environment.

Minimization of antibiotic usage can be attained by any number of means, including use of alternatives or use of synergists (probiotics/competitive exclusion products, phage therapy, enzyme therapy, vaccines, efflux pump inhibitors); improved animal husbandry and hygiene; minimization of OTC sales; continuing education for veterinary and health-care professionals, emphasizing environmental stewardship.

Needs: Integration of Cognitive Sciences with Environmental Sciences for the Communication of Risk

Critical that more resources be devoted to studying and improving the communication of risk to the general public (part of an overarching need to improve science literacy).

Need better understanding of the origins of the chasm existing between hazard/risk communication and how the public perceives risk. Especially important with the growing need to recycle water for drinking. This will prove critical in the coming years particularly for the "selling" to the public of "toilet-to-tap" water re-use projects. Maintenance of public trust in water supplies will prove critical.

Regardless of the thoroughness and soundness of the science that will continue to be developed, it will all be for naught without integrating the **cognitive sciences** (e.g., psychology) into the environmental sciences to develop a **better communications interface between science and the public.**

- concluded -

Some Example EPA Projects Relevant to Antibiotics in the Environment

- **STAR grants** (<http://www.epa.gov/nerlesd1/chemistry/pharma/star.htm>)
- Office of Water: Internal deliberations to include PPCPs on the CCL (**Contaminant Candidate List**: <http://www.epa.gov/safewater/ccl/cclfs.html>)
- **EPA's aquaculture project**. Much higher probability of parent compound being discharged directly to the environment. Similar to direct disposal of drugs. EPA's "Effluent Guidelines: Aquatic Animal Production Industry" (<http://www.epa.gov/waterscience/guide/aquaculture>)
- Office of Solid Waste internal initiative on pollution prevention via **pharmaceutical reverse distributors**
- Office of Research and Development's **PPCPs Web Site** (<http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm>)
- **Organizing and chairing of national symposia**
- In-house development of new environmental **chemical analysis tools**

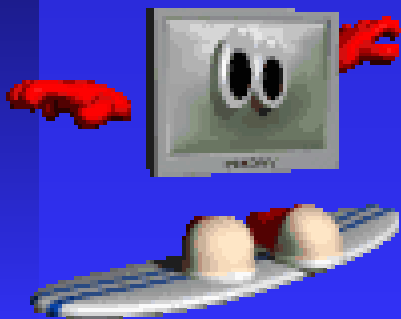
The Larger Picture

It is important to keep in mind that drugs used in agriculture (e.g., antimicrobials and anabolic steroids) represent only an unknown portion of the wide spectrum of PPCP classes that can occur as trace pollutants in the environment. The overall environmental issue is much larger and complex because of the great diversity of targeted therapeutic end-points coupled with a poorly defined universe of non-target effects, which in turn is amplified by a large number of non-target exposed species (especially in the aquatic environment).

The many issues involved in the larger issue are covered in EPA's PPCPs web site.

Wealth of other materials and links to ongoing work relevant to this broad topic are available at the U.S. EPA's **PPCPs Web Site:**

<http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm>





URL: <http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm>

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Pharmaceuticals and Personal Care Products (PPCPs) as Environmental Pollutants

Pollution from Personal Actions, Activities, and Behaviors

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➤ [NEW and prior work from the U.S. EPA ORD laboratory in Las Vegas](#)

➤ [Literature Citations Relevant to PPCPs in the Environment](#)

- NEW -- Book on Pharmaceuticals in the Environment, from the *American Chemical Society*
- NEW -- Book on Pharmaceuticals in the Environment, from *Springer-Verlag*
- NEW -- Discussions regarding the importance of the literature - *Literature Forensics*

➤ [Relevant and Useful Websites](#)

- NEW -- USGS Nationwide Water Monitoring Program (including PPCPs)

➤ [Media Coverage of EPA Activities in PPCPs](#)

➤ [Scientific Conferences Devoted to PPCPs in the Environment](#)

- Assistance with Conferences, Seminars, or Lectures

➤ [Listing of Scientists Involved with Environmental Aspects of PPCPs](#)



➤ [Research Needs and Gaps](#)

➤ [Grants Awarded for Research on PPCPs](#)

➤ [Opportunities for Funding and for Research in Collaboration with EPA Scientists](#)

➤ [Communicating Science and Science Literacy](#)

➤ [Teaching Environmental Science -- Guide to Relevant Materials on PPCPs](#)

➤ [EPA's Terms of Environment \(glossary of technical terminology\)](#)

➤ [Environmental Chemistry: Measurement - Methods - Quality Assurance - Statistics](#)



Origins and fate of PPCPs in the Environment



Questions?



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<http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm>



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Institute of Medicine (IOM)

Roundtable on Environmental Health
Sciences, Research, and Medicine
<http://www.iom.edu/iom/iomhome.nsf>

Roundtable #9: *Human Health Effects of Using
Antimicrobial Agents in Agriculture*

9 December 2002, Washington, DC

prepared for:

**National Academy of Sciences' Institute of
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9 December 2002
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